



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUN 3 1999

MEMORANDUM

OFFICE OF
SOLID WASTE AND EMERGENCY
RESPONSE

SUBJECT: Release of Report on Perchlorate Toxicity Peer Review

FROM: Timothy Fields, Jr. *Timothy Fields, Jr.*
Acting Assistant Administrator
Office of Solid Waste and Emergency Response

TO: Interested Parties

Please find the attached final report of the external peer review workshop on the toxicity of perchlorate, held on February 10-11, 1999, in San Bernardino, California. The peer review workshop was conducted by Research Triangle Institute, a contractor to EPA's Office of Solid Waste and Emergency Response. Areas covered by the peer review included the draft toxicological review document for perchlorate, protocols and results of several recently completed and ongoing toxicological and ecological effects studies on perchlorate, and the harmonized human health oral risk benchmark (RfD) proposed for perchlorate in the toxicological review document.

The peer review workshop was sponsored by the EPA Office of Solid Waste and Emergency Response (OSWER) and Office of Water. The draft toxicological review document for perchlorate, entitled "Perchlorate Environmental Contamination: Toxicological Review and Risk Characterization Based on Emerging Information", was prepared by EPA's National Center for Environmental Assessment (NCEA). The draft toxicological review document presented an updated human health risk assessment as well as a screening ecological assessment of newly performed studies on perchlorate. The updated human health assessment harmonizes noncancer and cancer approaches to derive a single proposed oral RfD based on precursor effects for both non-cancer health effects and thyroid cancer.

The panel concluded that the presentation of the data in the toxicological review document was generally well done but that further work is needed before the RfD proposed by EPA can be definitively evaluated. It recommended using thyroid hyperplasia (increase in cell number) rather than thyroid hypertrophy (increase in cell size) for the determination of the reference dose, since it concluded that hypertrophy is an adaptive effect, not an adverse effect. The panel recommended that a pathology working group (PWG) be convened to review the thyroid and brain tissue from all previous and pending studies. This PWG review will provide for a common nomenclature of lesions and for a consistent pathology review across studies. In addition, the peer reviewers identified a number of statistical issues that should be addressed by NCEA.

The peer reviewers commended NCEA's use of available biological and toxicological data to move in the direction of a harmonized approach to assessing cancer and noncancer endpoints,

and encouraged further use of the mode of action data in the determination of the RfD. The peer reviewers concluded that the RfD proposed by EPA in the toxicological review document (0.0009 mg/kg/d) is likely to be conservative, based upon the existing toxicological data base.

The panel found that the ecotoxicology studies were well done and support the screening ecological risk assessment. The major weaknesses of the screening ecological risk assessment (SERA) were identified as limited data on the current levels of perchlorate in the environment and the potential for long-term effects. These data limitations resulted in a SERA that was conservative both in terms of the risk-based effects thresholds suggested and the scope of the additional studies recommended. The lack of this information makes it difficult to determine what types of fish, wildlife and plants are at risk from perchlorate.

NCEA is currently working with the National Institute of Environmental Health Sciences on the establishment of a PWG to review the thyroid and brain tissue from all previous and pending studies. In the final toxicological review document, NCEA will address comments made in the peer review workshop report, and will review and incorporate data from additional studies that are currently ongoing, as well as the results of the PWG review.

Several months ago the Agency committed to a second external peer review as part of the process to characterize the potential human and ecotoxicological risks associated with perchlorate contamination. The purpose of the second external peer review will be to evaluate the additional data, the presentation and analyses of these data in the toxicological review document, and the draft final NCEA assessment. It is anticipated that a second peer review workshop will be held early in 2000. The second peer review may use a number of the peer reviewers that participated in the recent workshop. This next peer review is intended as part of the Integrated Risk Information System (IRIS) process. After revision to reflect any additional comments or recommendations, the final NCEA assessment will then go to IRIS consensus review.

EPA's Office of Research and Development will address in a separate memorandum the issue of the appropriate provisional reference dose for perchlorate pending the completion of the final toxicological review document with its associated health benchmark dose. In brief, it will recommend the continued use of the existing provisional reference dose range of 0.0001 to 0.0005 mg/kg-day, until such time as a final benchmark is approved.

Any questions regarding the peer review workshop report should be directed to Peter Grevatt (202-260-3100) or Dorothy Canter (202-260-2230) of my staff.

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